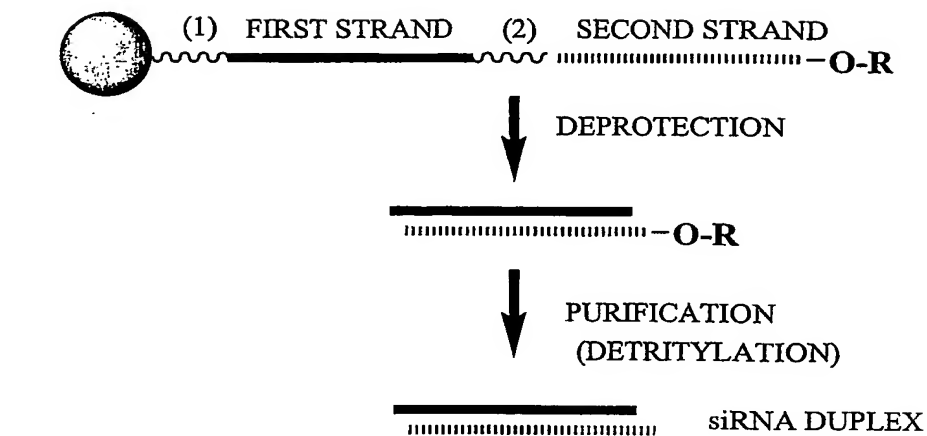


1/25

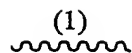
Figure 1

= SOLID SUPPORT

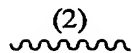
R = TERMINAL PROTECTING GROUP

FOR EXAMPLE:

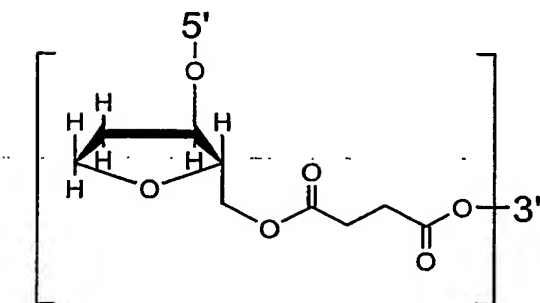
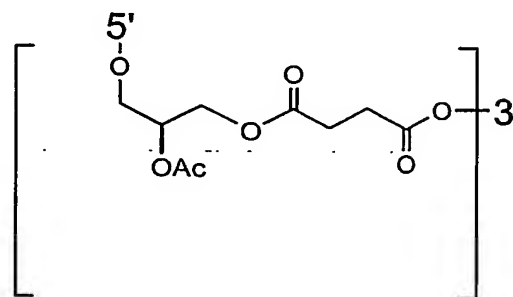
DIMETHOXYTRITYL (DMT)



(1) = CLEAVABLE LINKER

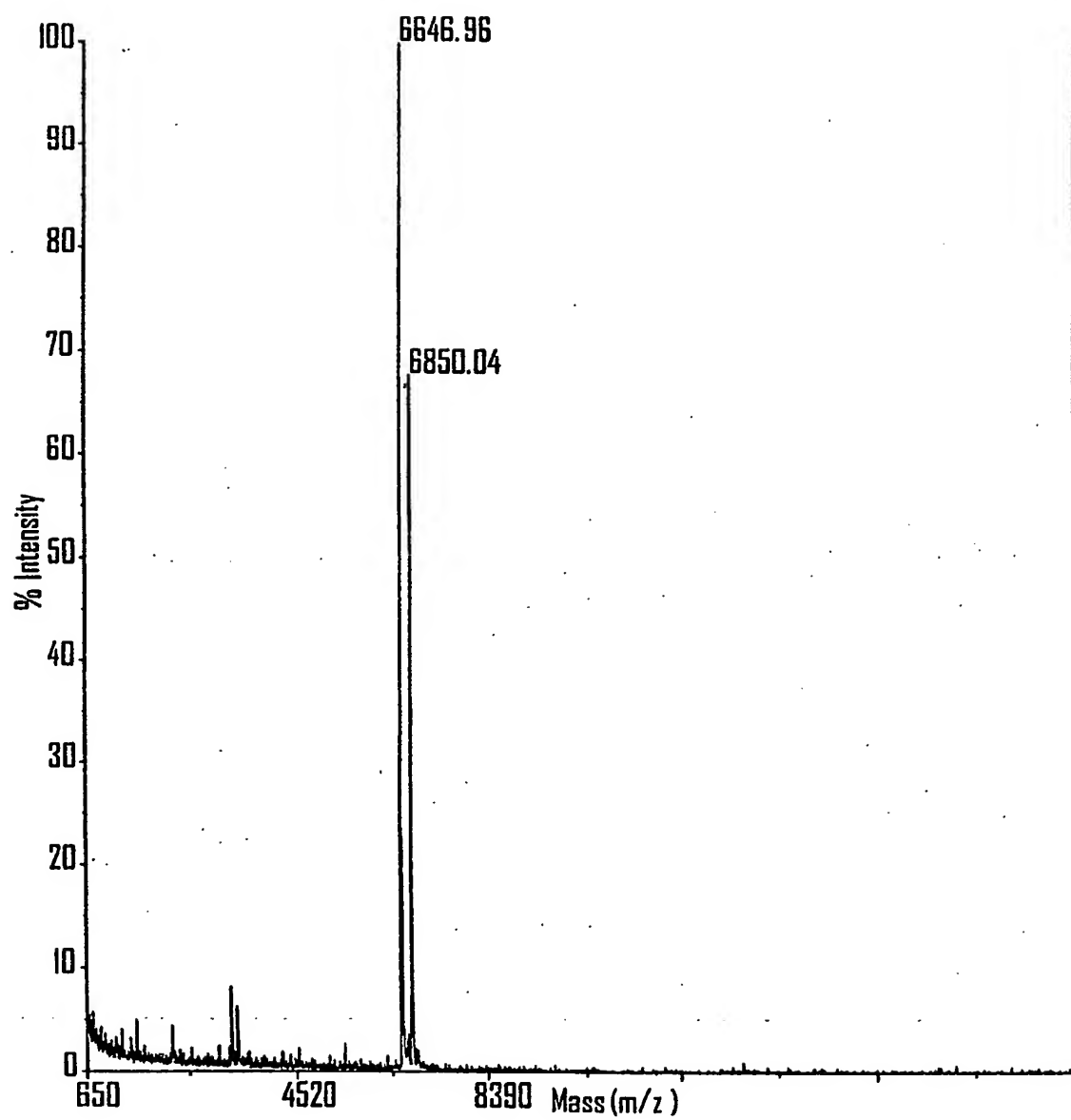
(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)

(2) = CLEAVABLE LINKER

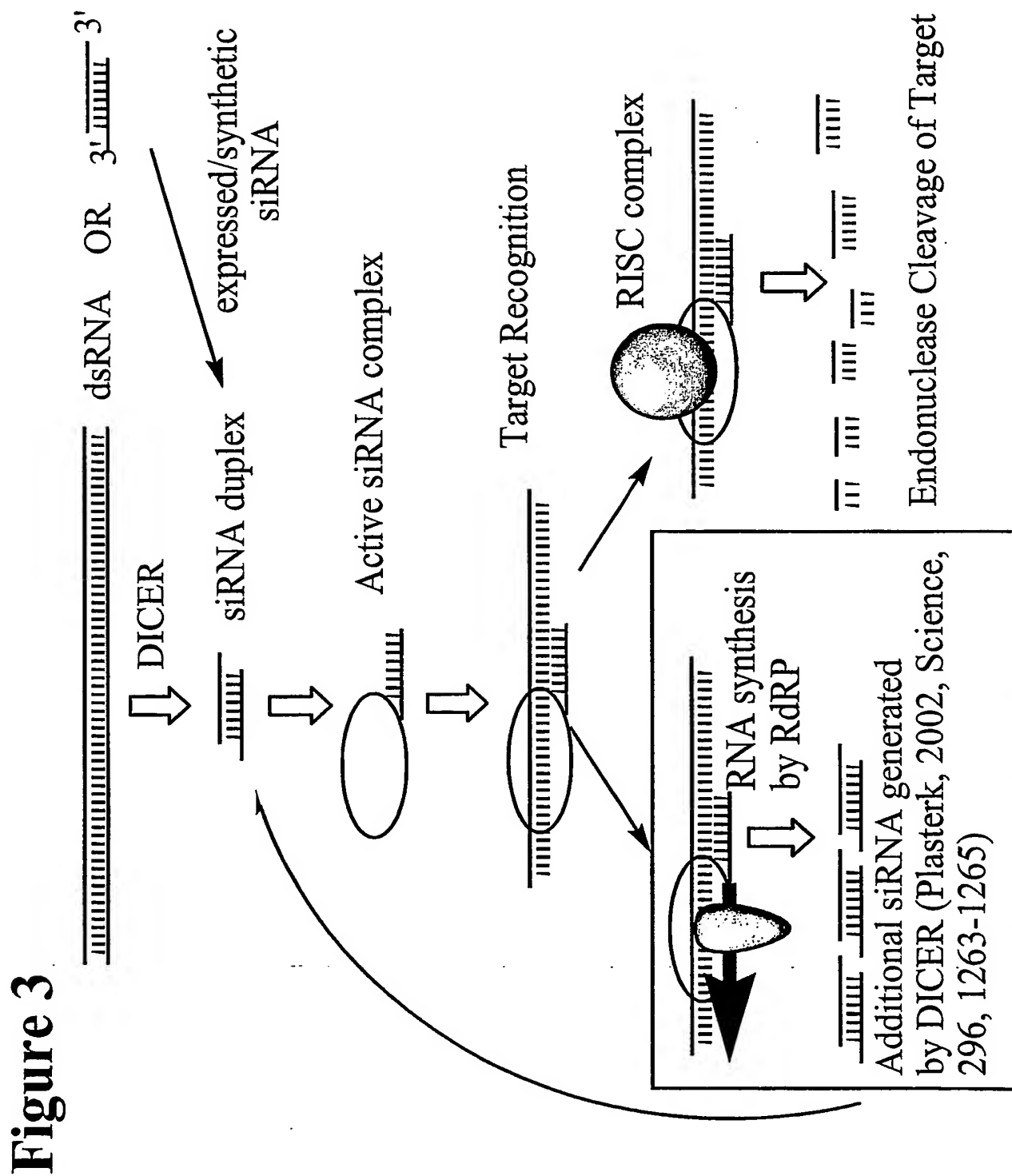
(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)INVERTED DEOXYABASIC SUCCINATE
LINKAGE

GLYCERYL SUCCINATE LINKAGE

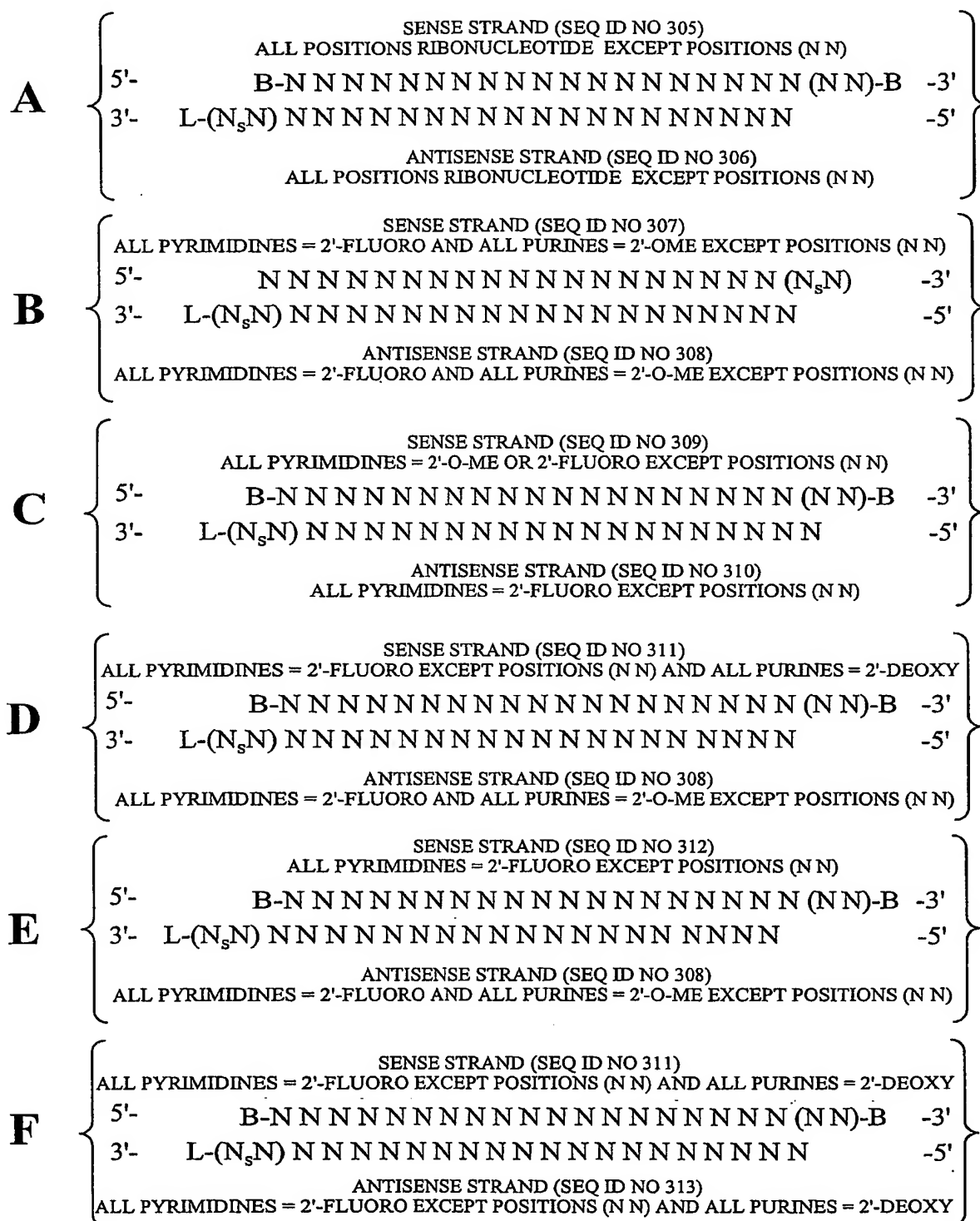
2/25

Figure 2

3/25



4/25

Figure 4

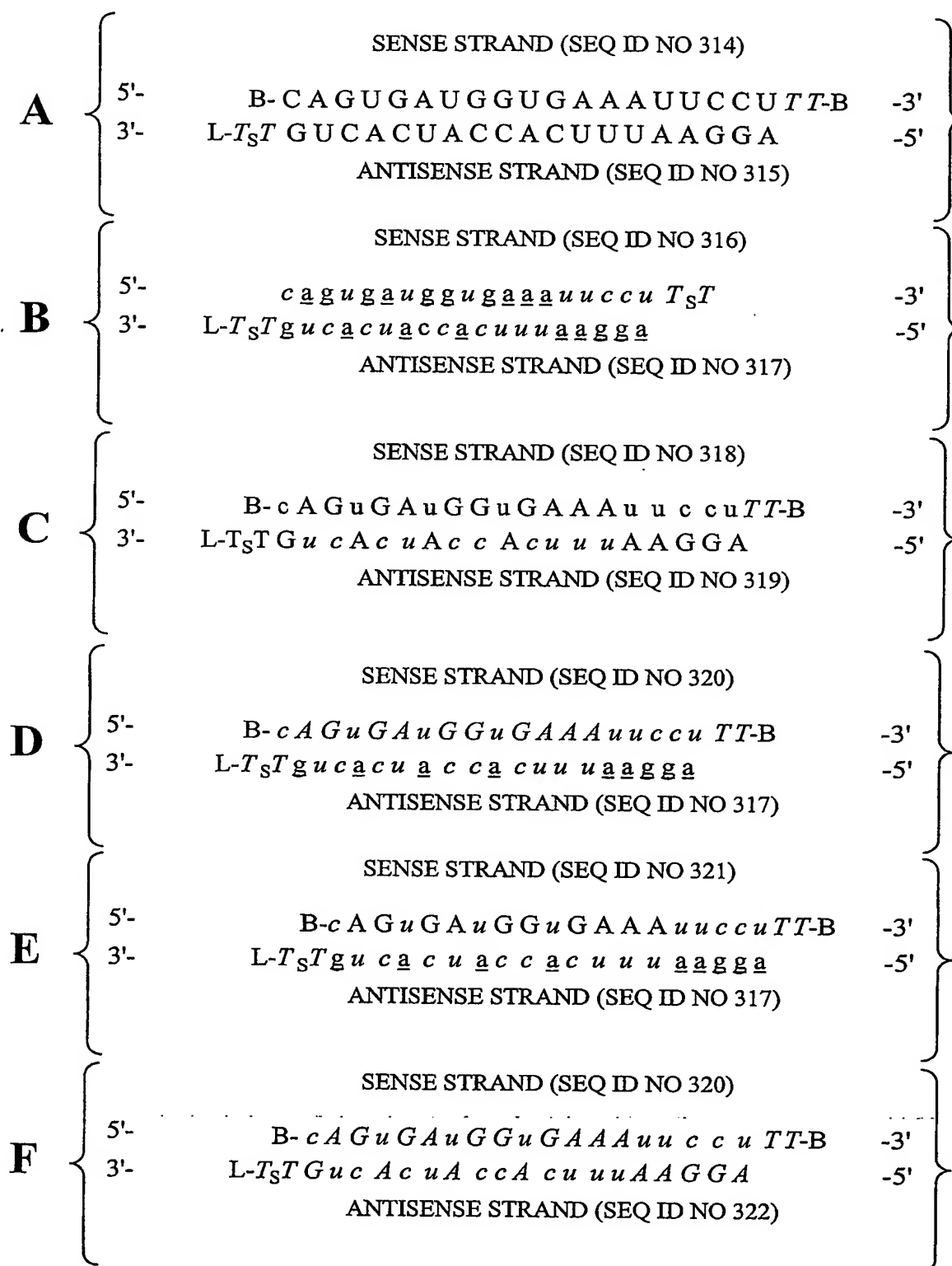
POSITIONS (NN) CAN COMPRISE ANY NUCLEOTIDE, SUCH AS DEOXYNUCLEOTIDES (eg. THYMIDINE) OR UNIVERSAL BASES

B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP THAT IS OPTIONALLY PRESENT

L = GLYCERYL or B THAT IS OPTIONALLY PRESENT

S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE THAT IS OPTIONALLY PRESENT

5/25

Figure 5

lower case = 2'-O-Methyl or 2'-deoxy-2'-fluoro

italic lower case = 2'-deoxy-2'-fluorounderline = 2'-O-methyl

ITALIC UPPER CASE = DEOXY

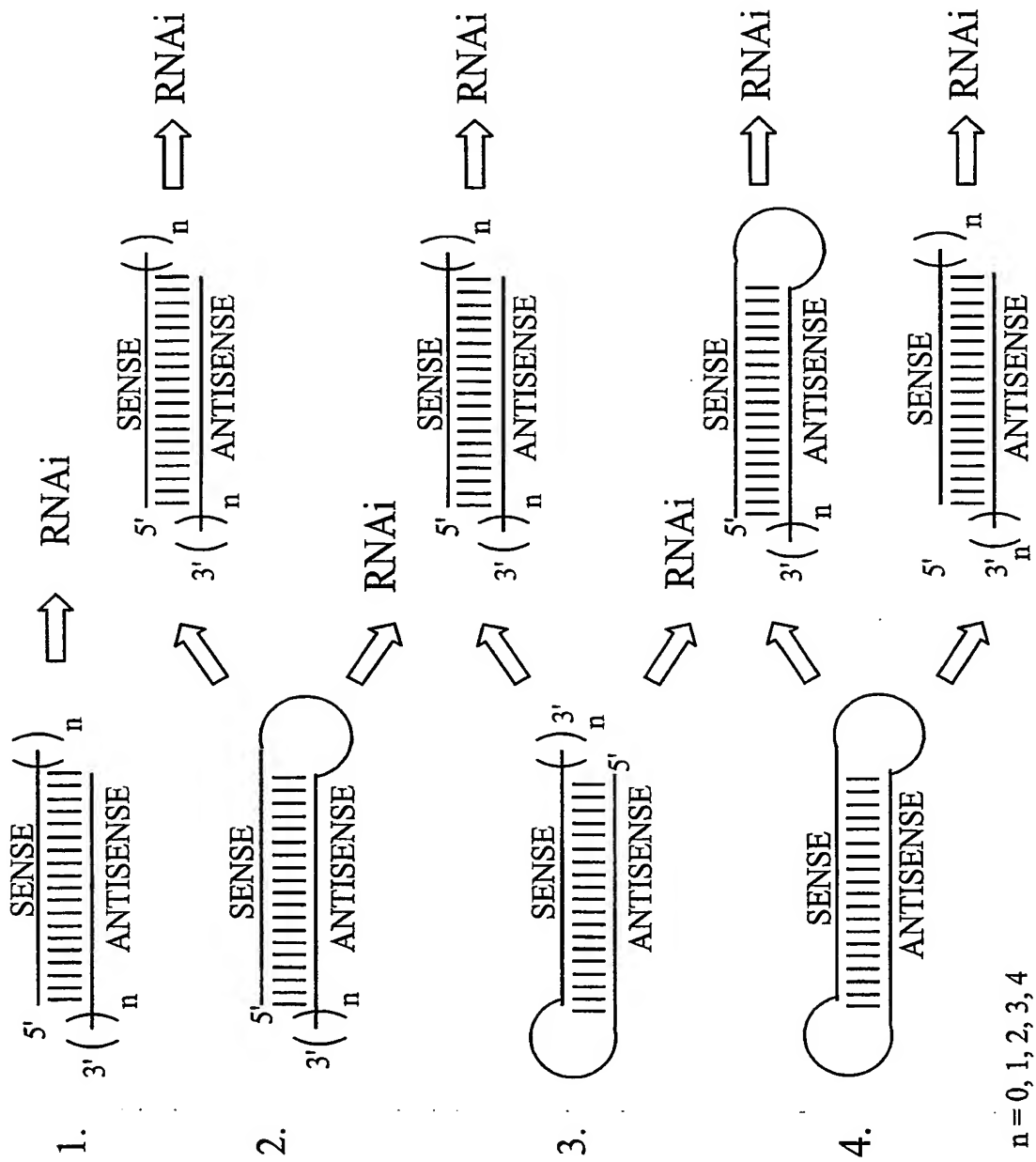
L = GLYCERYL MOIETY OR IS OPTIONALLY PRESENT

B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE, OR OTHER TERMINAL CAP THAT IS OPTIONALLY PRESENT

S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE OPTIONALLY PRESENT

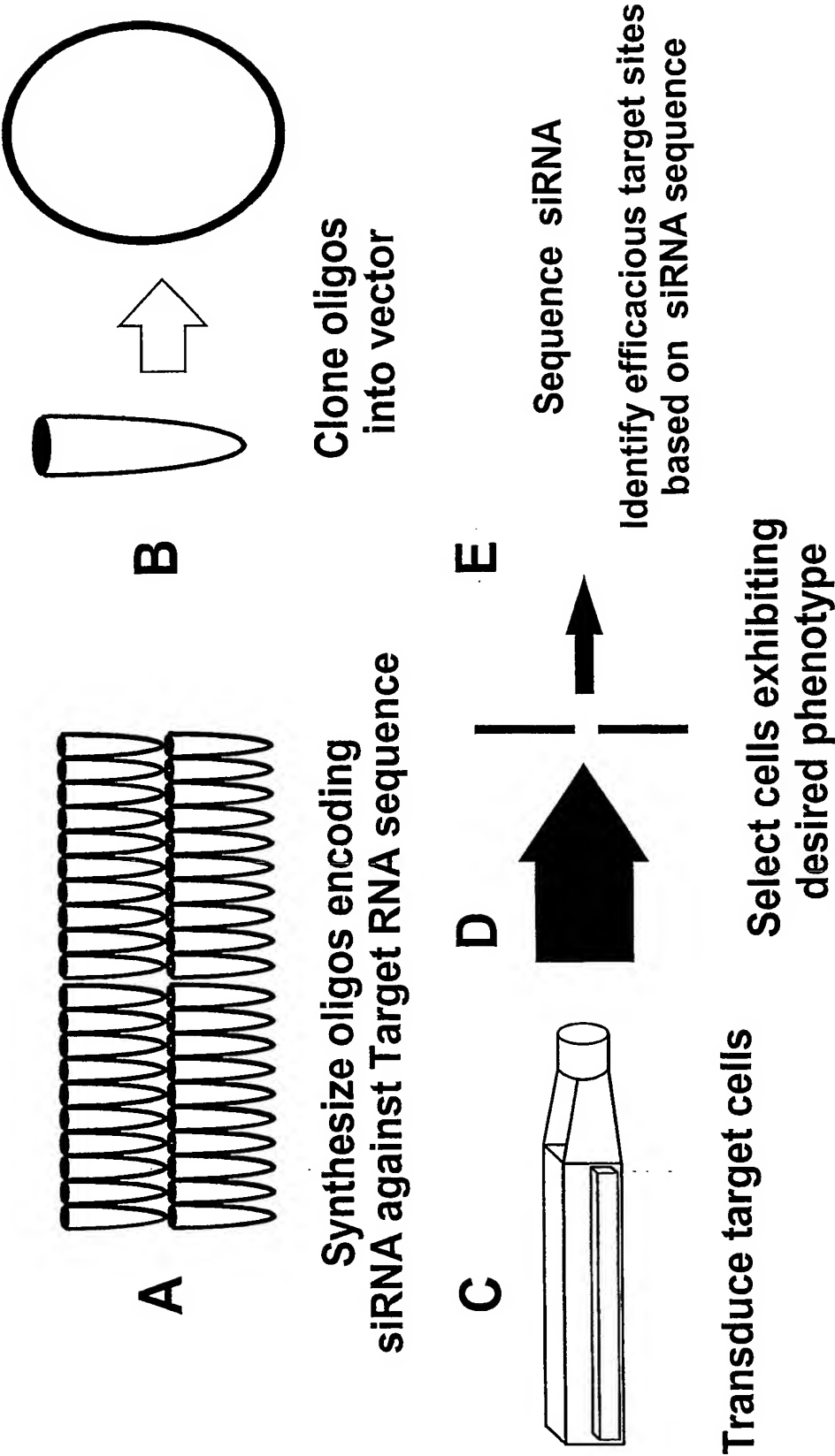
6/25

Figure 6

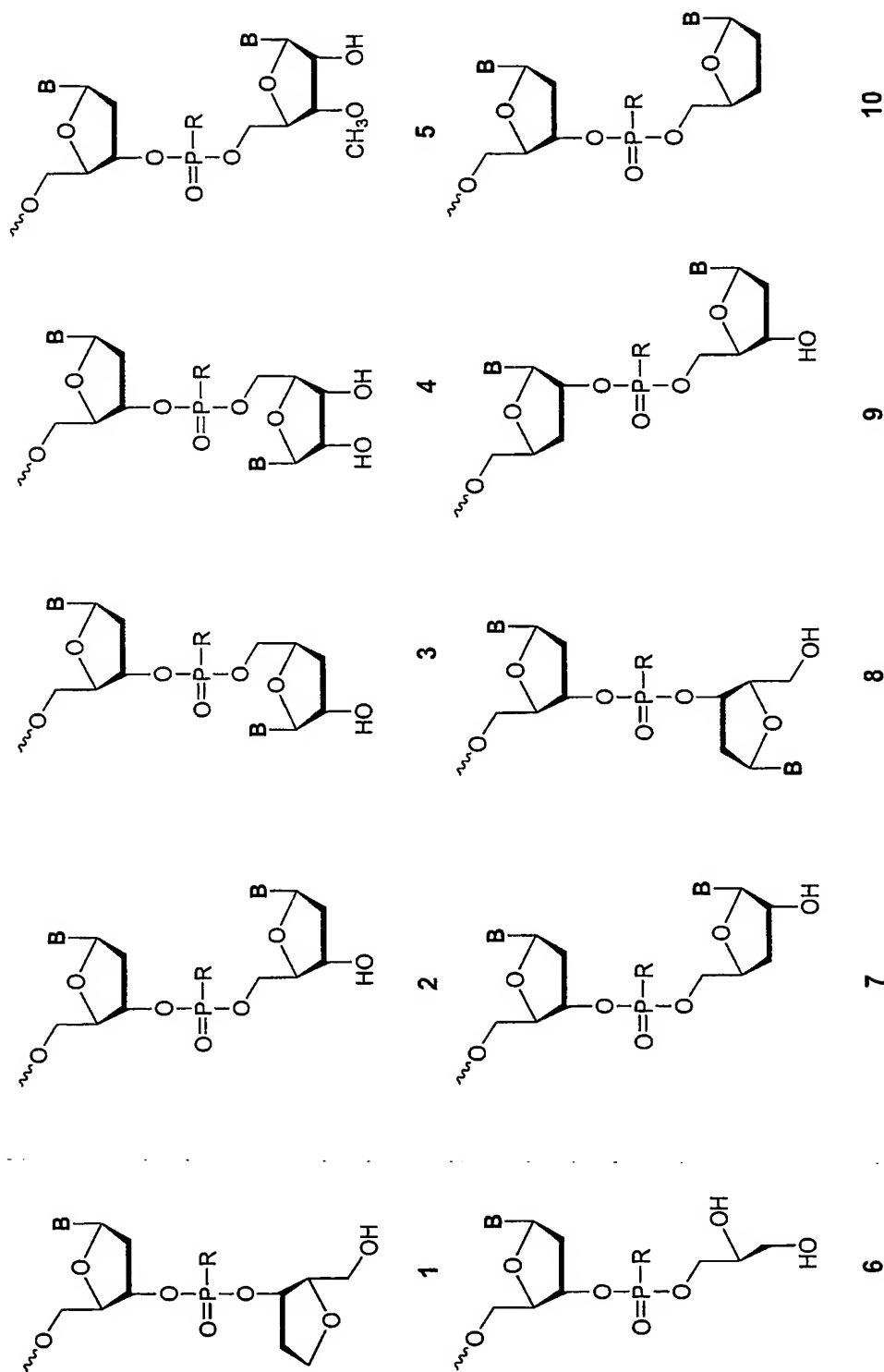


9/25

Figure 9: Target site Selection using siRNA

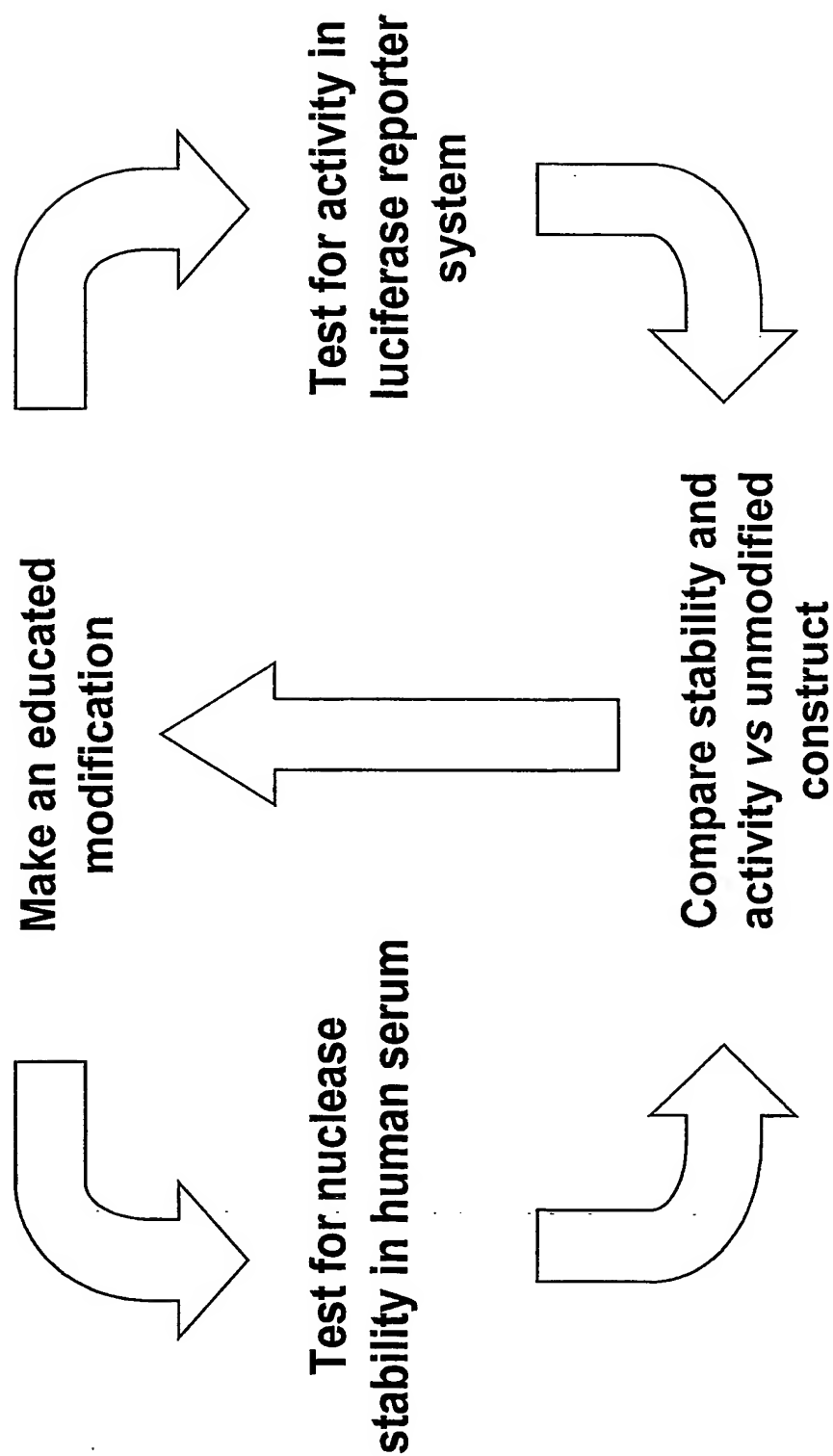


10/25

Figure 10

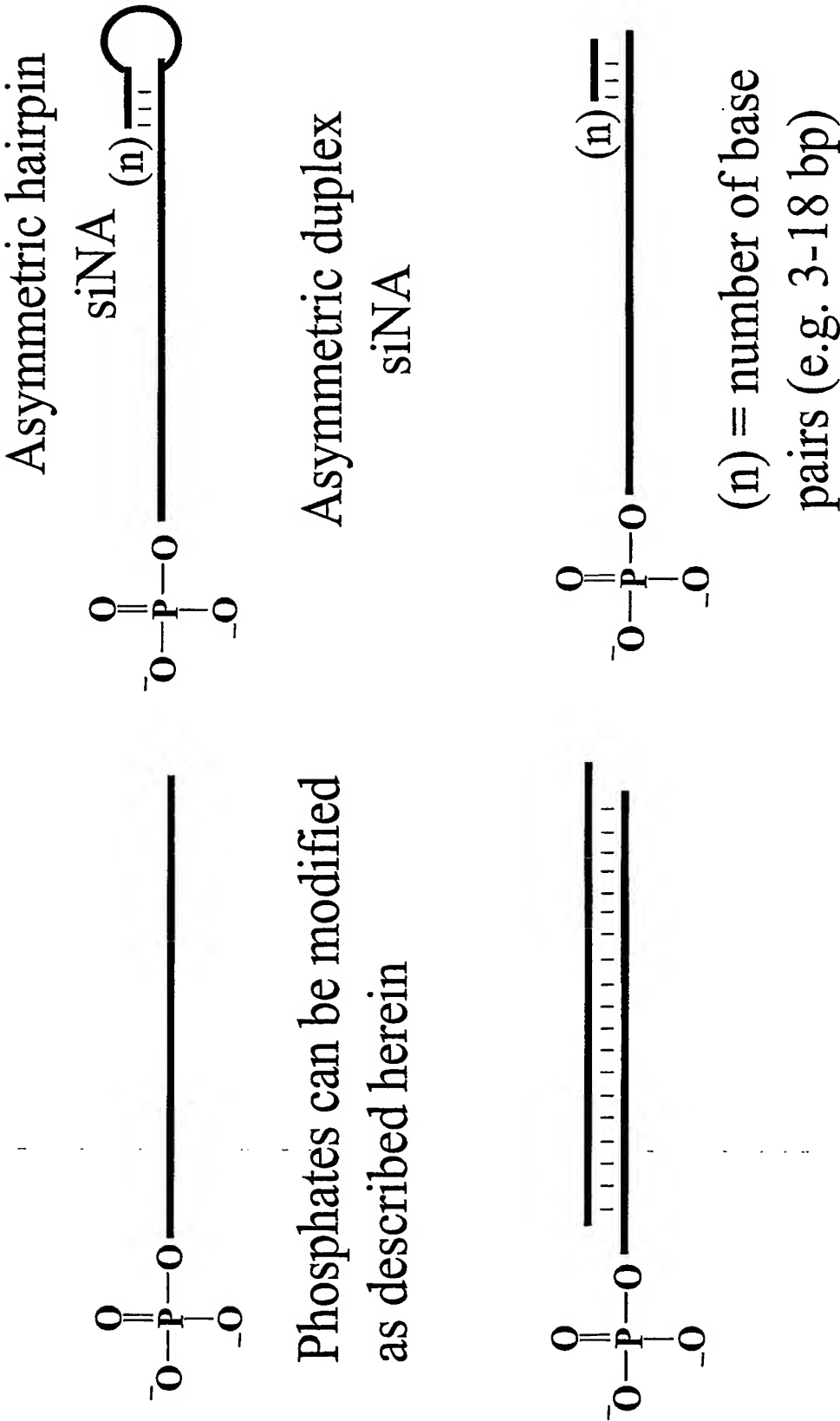
R = O, S, N, alkyl, substituted alkyl, O-alkyl, S-alkyl, alkaryl, or aralkyl
B = Independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).

11/25

Figure 11: Modification Strategy

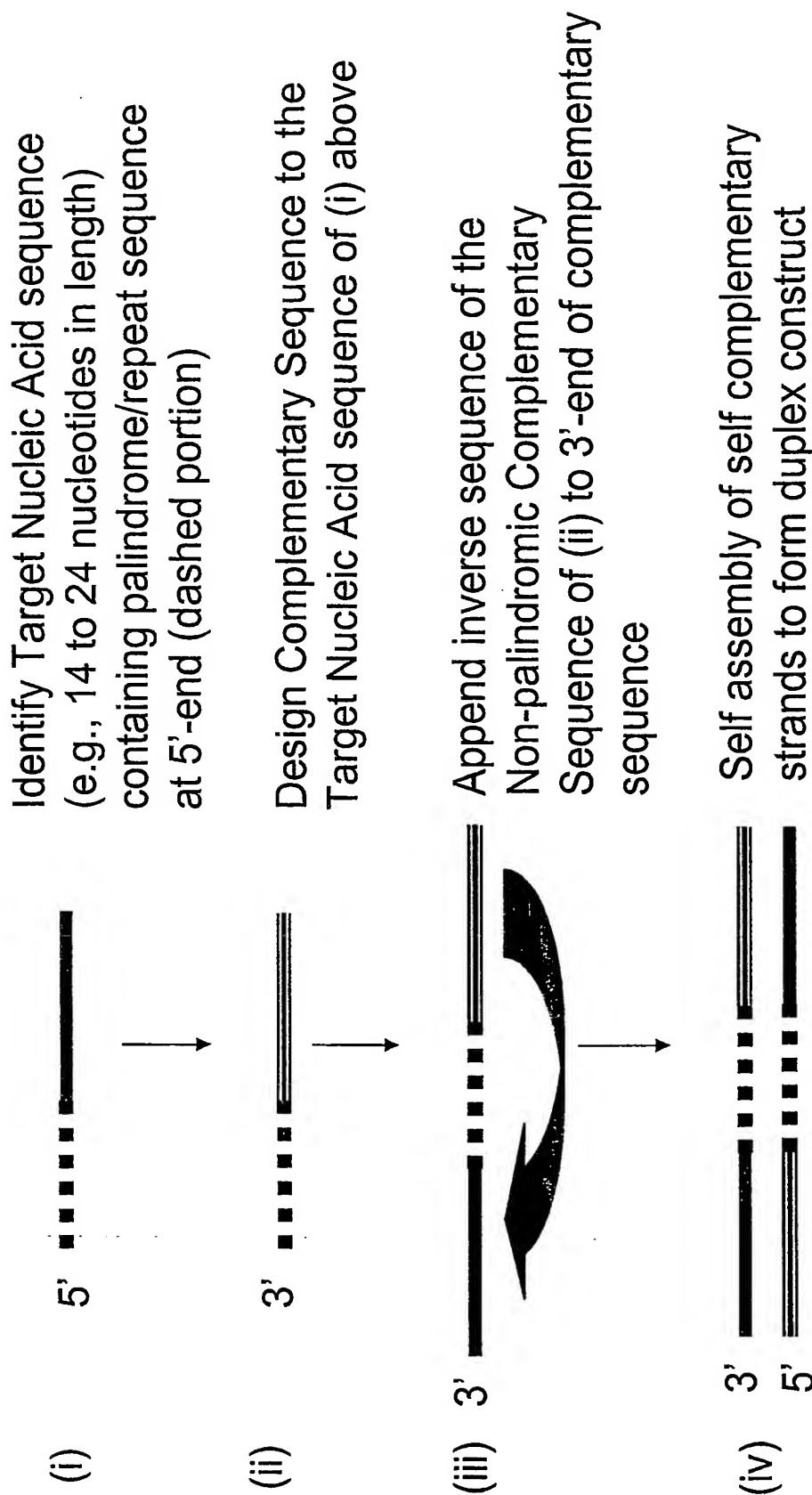
12/25

Figure 12: Phosphorylated siNA constructs



14/25

Figure 14A: Duplex forming oligonucleotide constructs that utilize Palindrome or repeat sequences



15/25

Figure 14B: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence

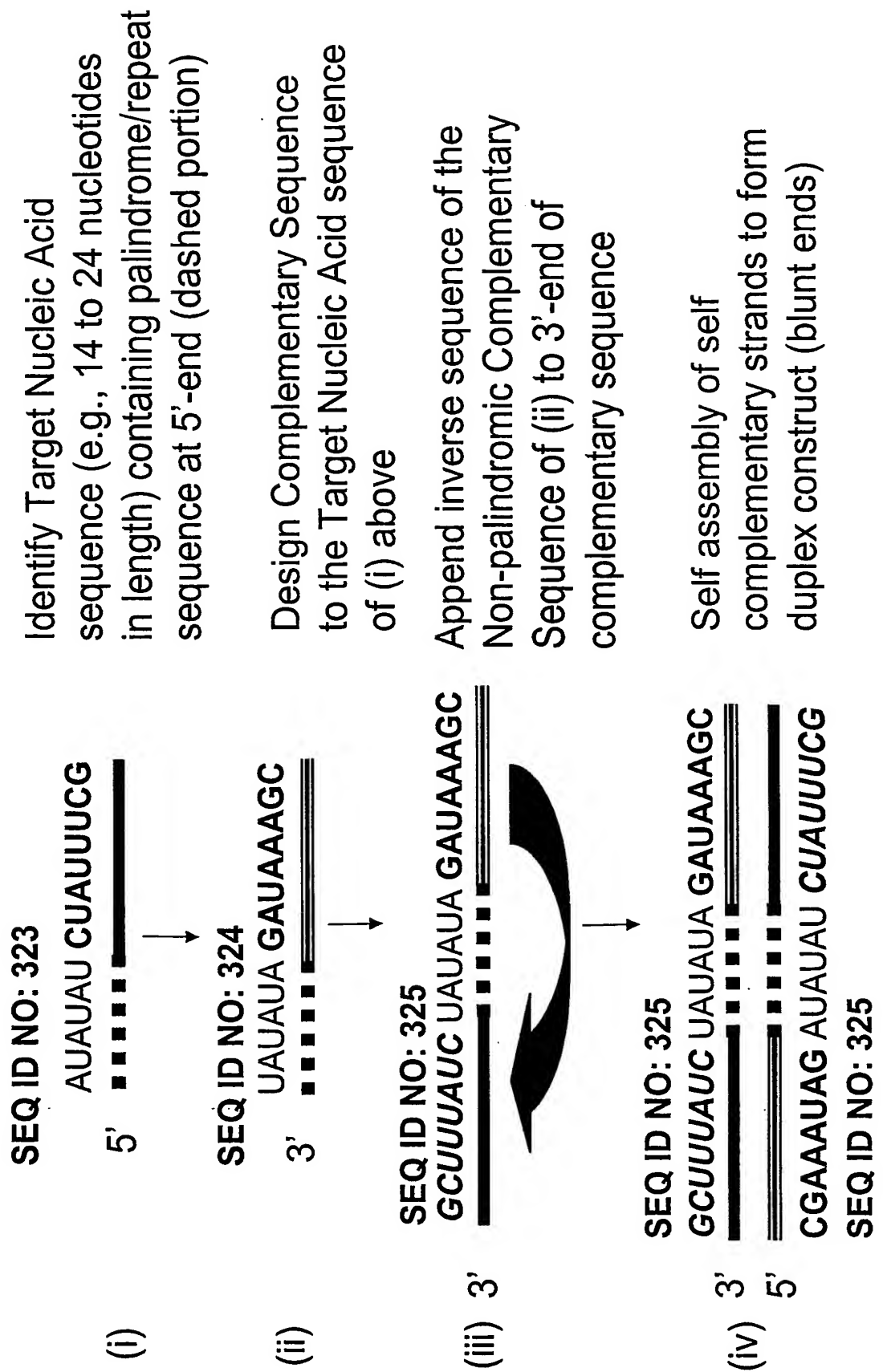


Figure 14C: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly

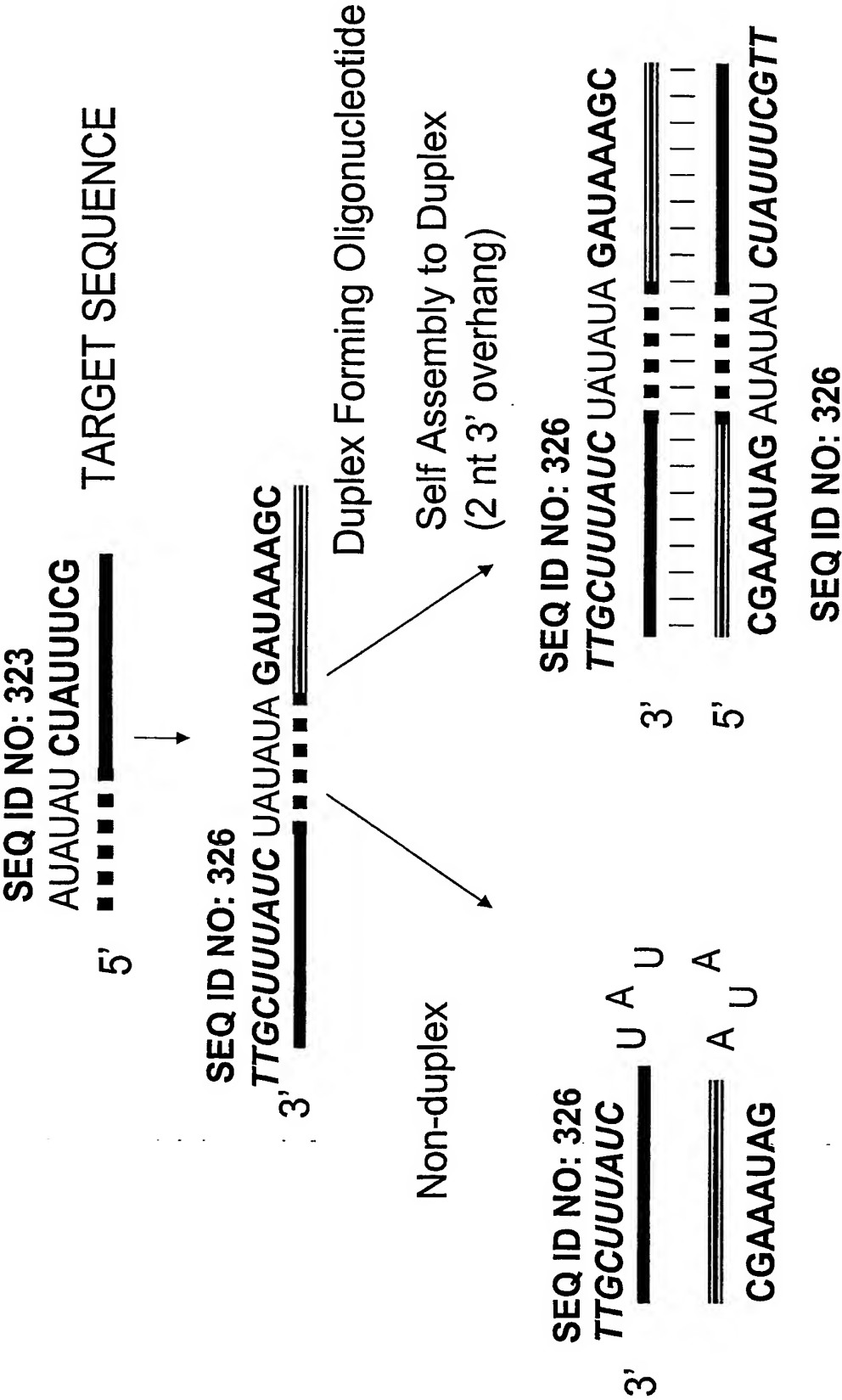


Figure 15: Duplex forming oligonucleotide constructs that utilize artificial palindrome or repeat sequences

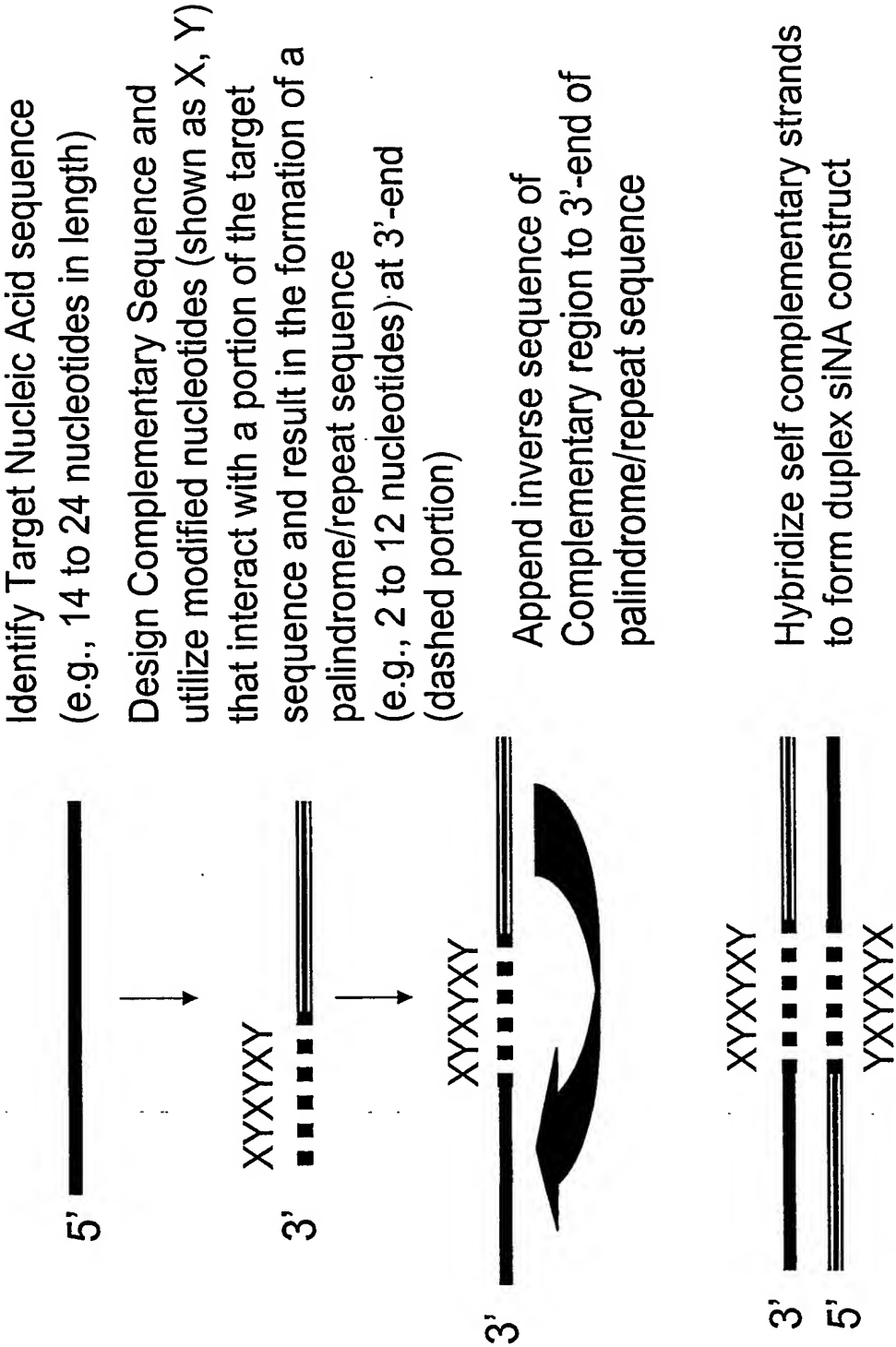
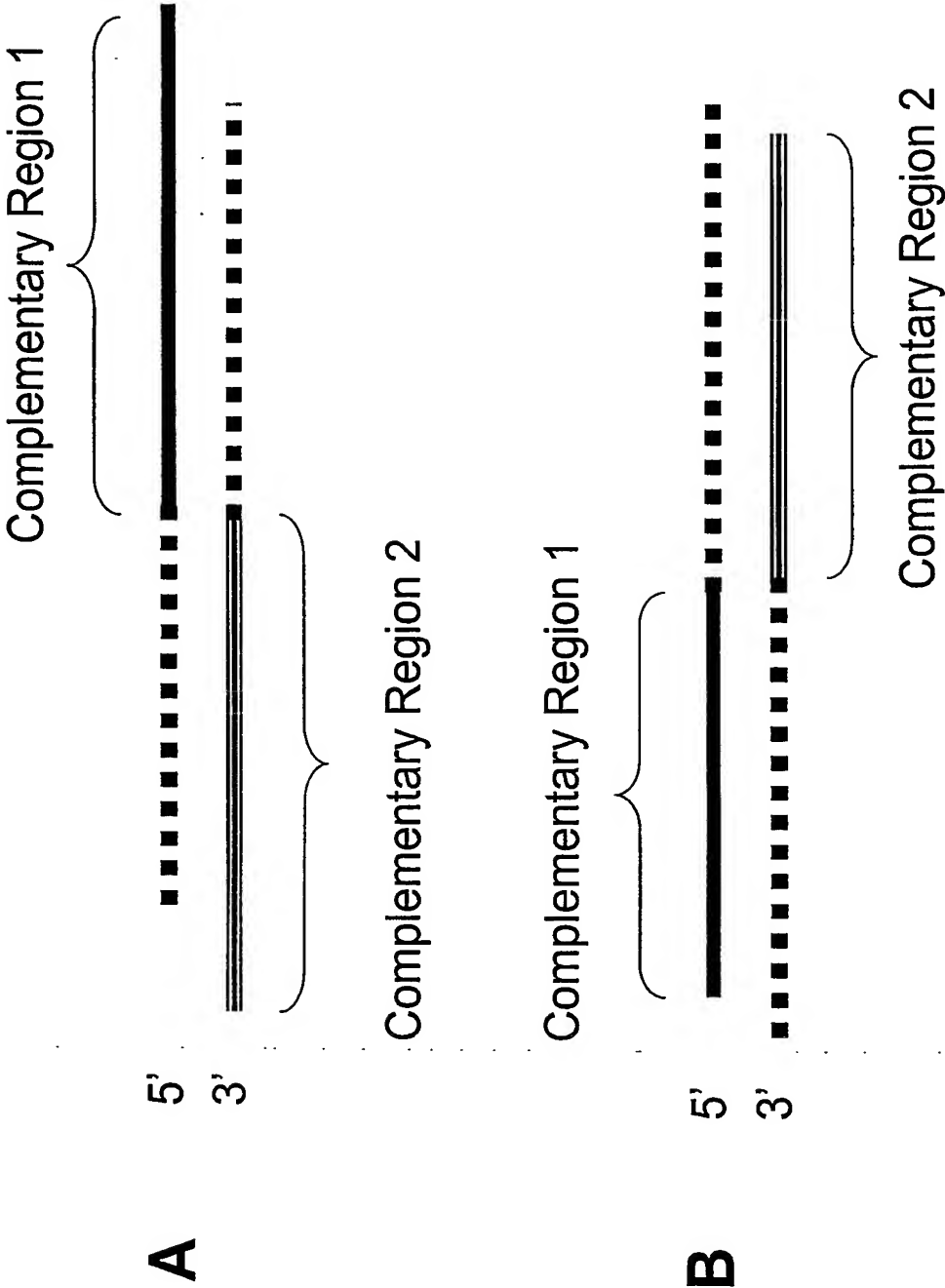


Figure 16: Examples of double stranded multifunctional siNA constructs with distinct complementary regions



20/25

Figure 17: Examples of hairpin multifunctional siNA constructs with distinct complementary regions

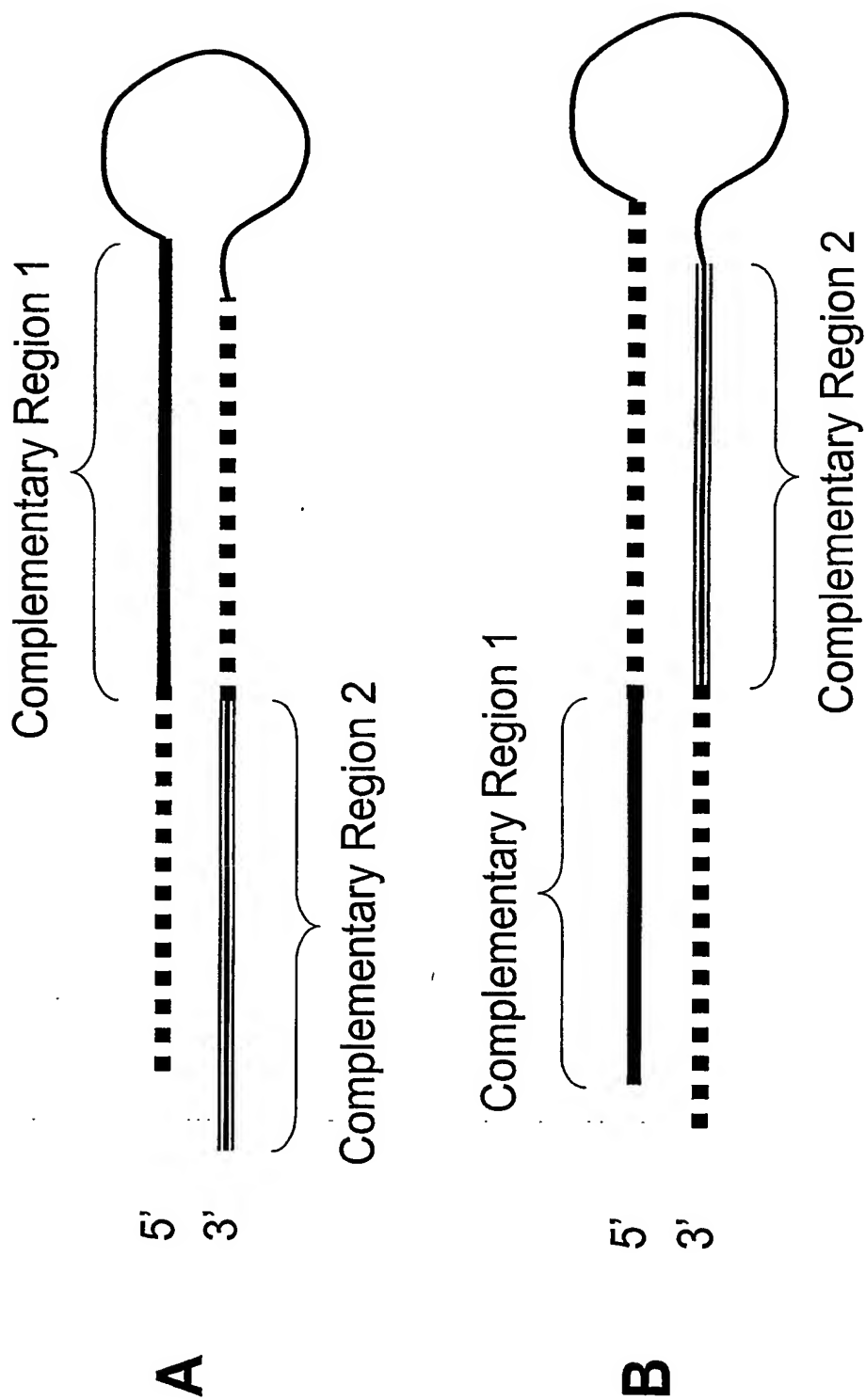


Figure 18: Examples of double stranded multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region

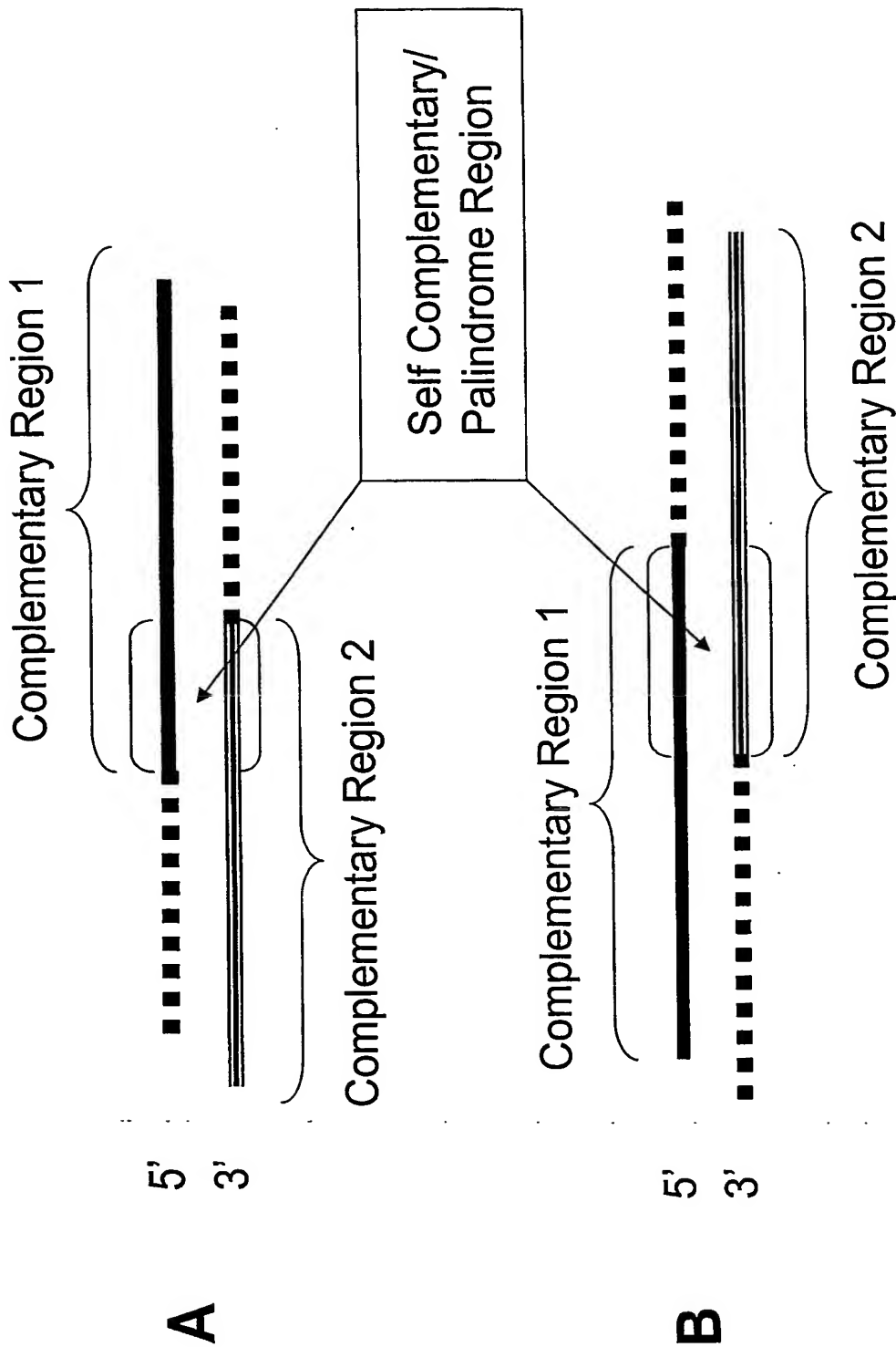
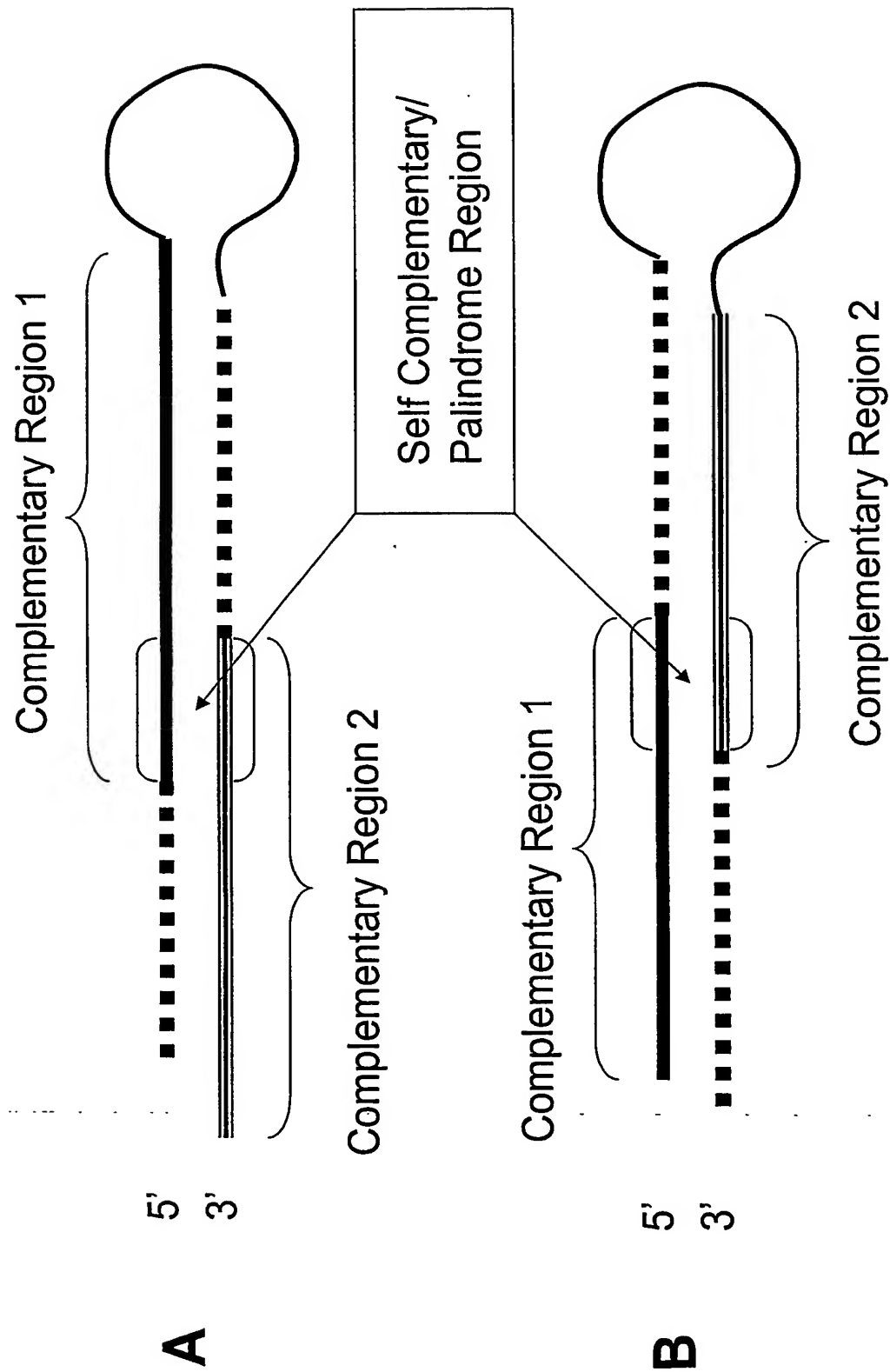


Figure 19: Examples of hairpin multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region



**Figure 20: Example of multifunctional siRNA targeting two
Separate Target nucleic acid sequences**

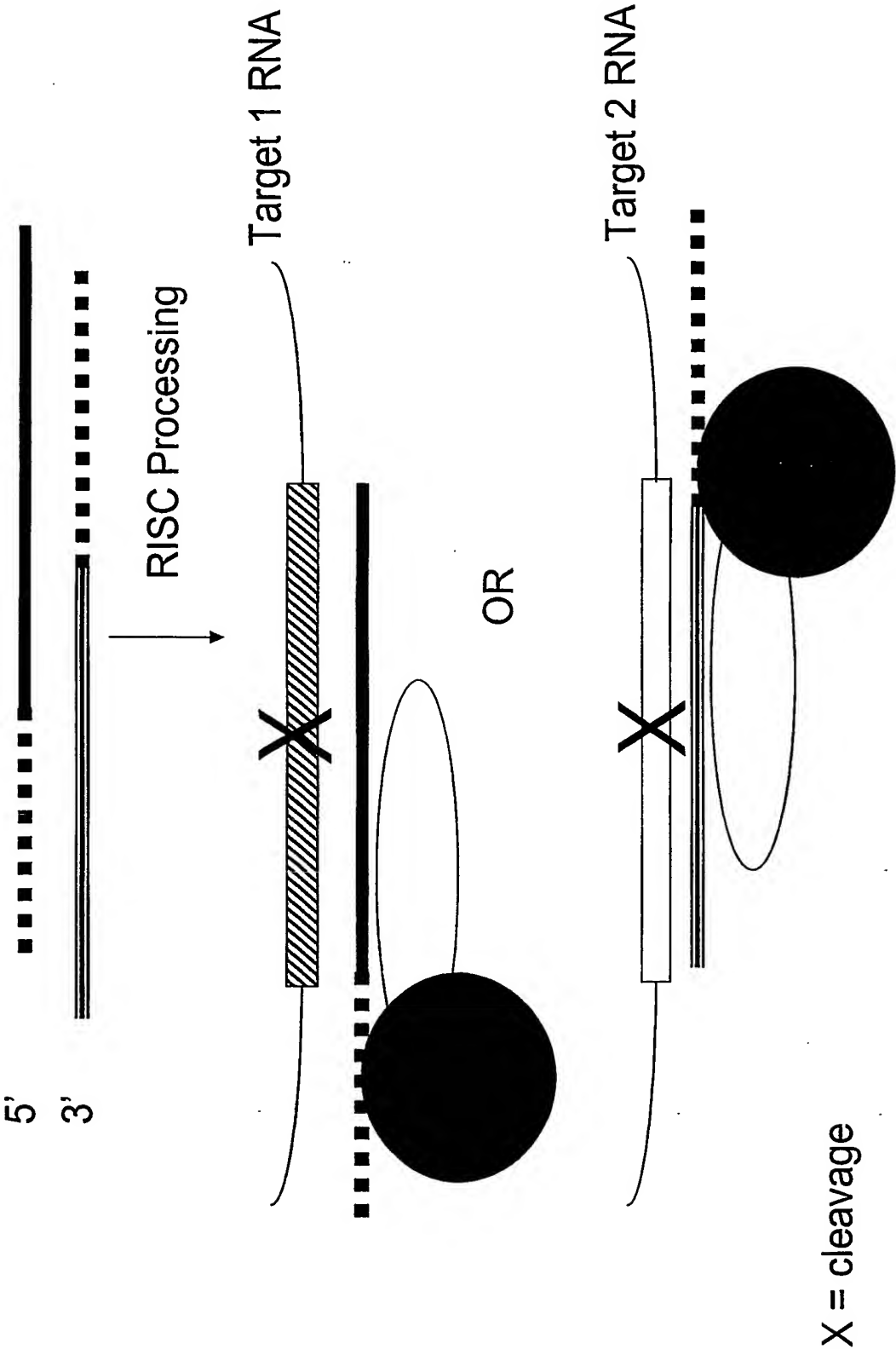
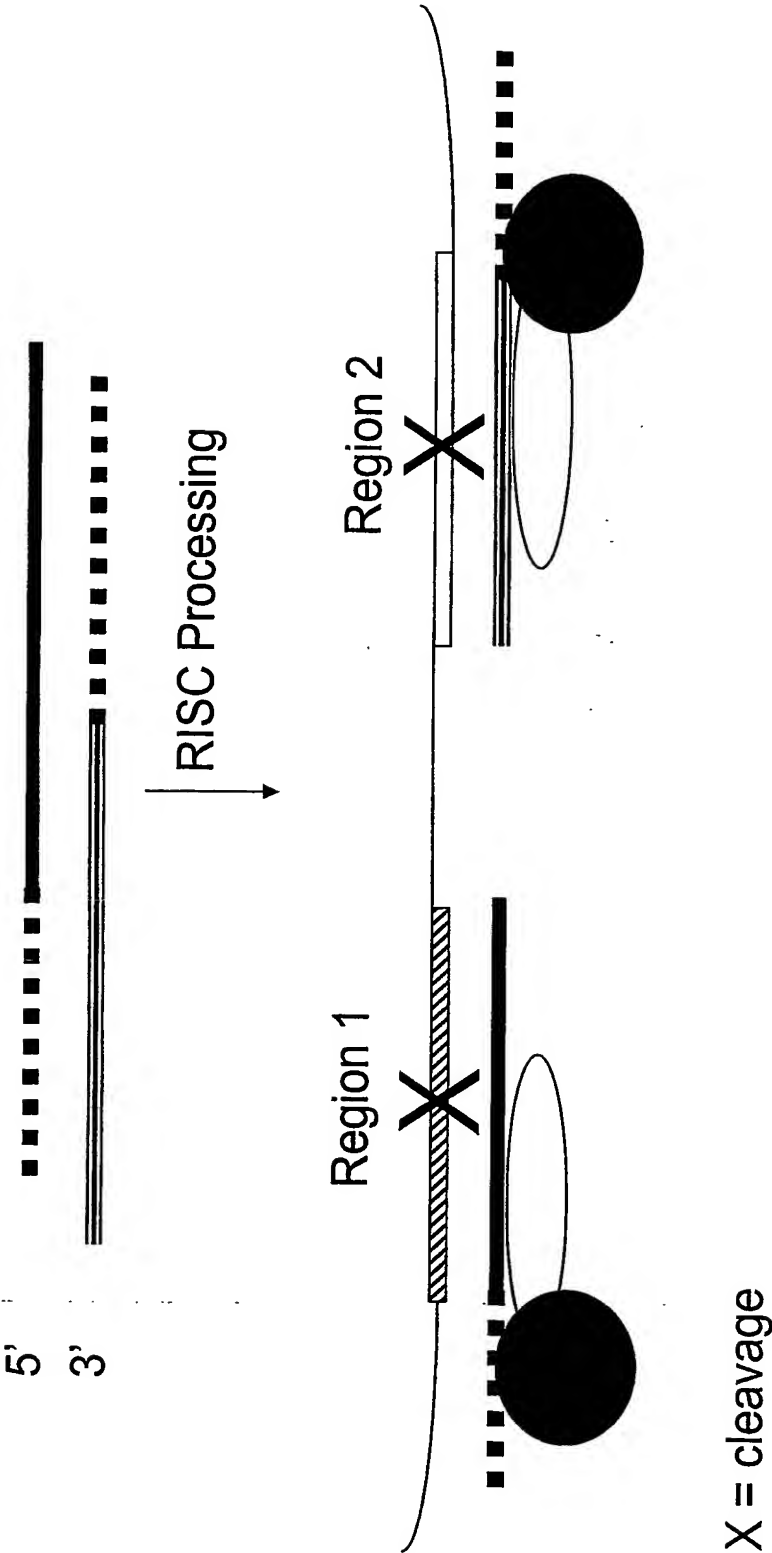


Figure 21: Example of multifunctional siNA targeting two regions within the same target nucleic acid sequence



25/25

FIGURE 22

